REMARKS

I. INTRODUCTION

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

Claims 1-77 were previously canceled.

Claims 84, 90, 115 and 117 are currently being amended.

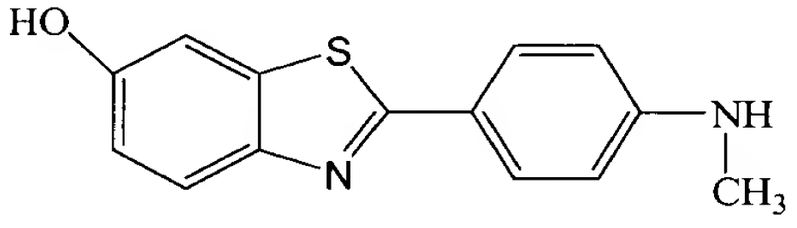
This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

After amending the claims as set forth above, claims 78-130 are now pending in this application.

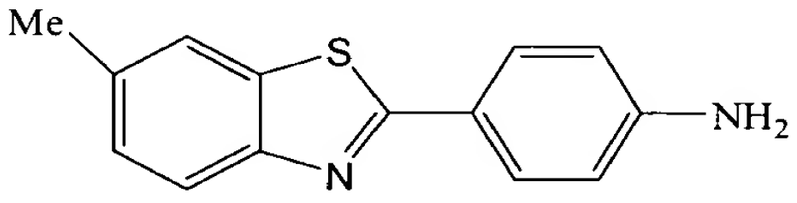
II. THE OFFICE ACTION

A. Clarification of Record

The Examiner explains in the Office Action on pages 2-4 the reasons for searching the elected species having the following structure:



which is encompassed by independent claim 84, and then choosing to search the following species:

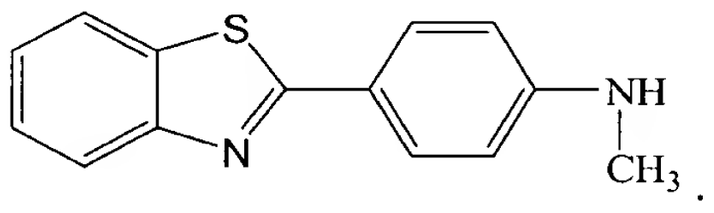


which is not encompassed by independent claim 84. Rather, the Examiner has searched for the above compound and rejected claim 81 based on prior art. It appears that the Examiner has ignored the very section of the MPEP to which she refers. The Examiner cites to MPEP 803.02, as quoted on page 3 of the Office Action: "[i]n MPEP 803.02, it is disclosed that

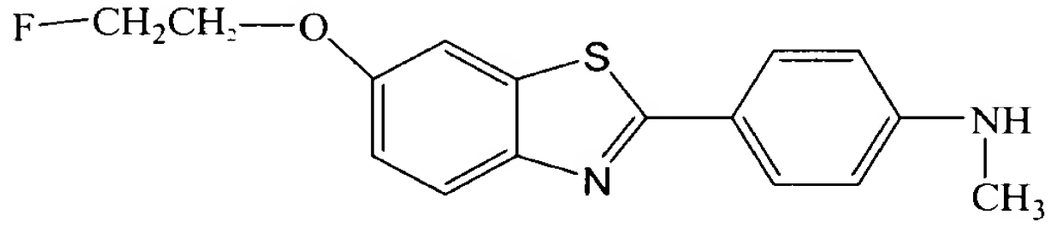
should no prior art be found that anticipates or renders obvious the elected species, then the search of the Markush type claim will be extended."

In the present case, the Examiner has not extended the search of claim 84, rather, she has extended the search to the above compound without extending the search of the Markush type claim, i.e., claim 84. Since the elected species is encompassed by the Markush structure of claim 84, according to MPEP 803.02, it appears that the search of claim 84 should be extended. In the present case, the Examiner chose a species which is encompassed by a different Markush type claim, claim 81, and searched that species. The present claim set contains more than one species claim which is dependent upon claim 84, i.e., claims 91 and 104 (in addition to claim 106, the elected species). The compounds corresponding to claims 91 and 104 have the following chemical structures:

Claim 91:

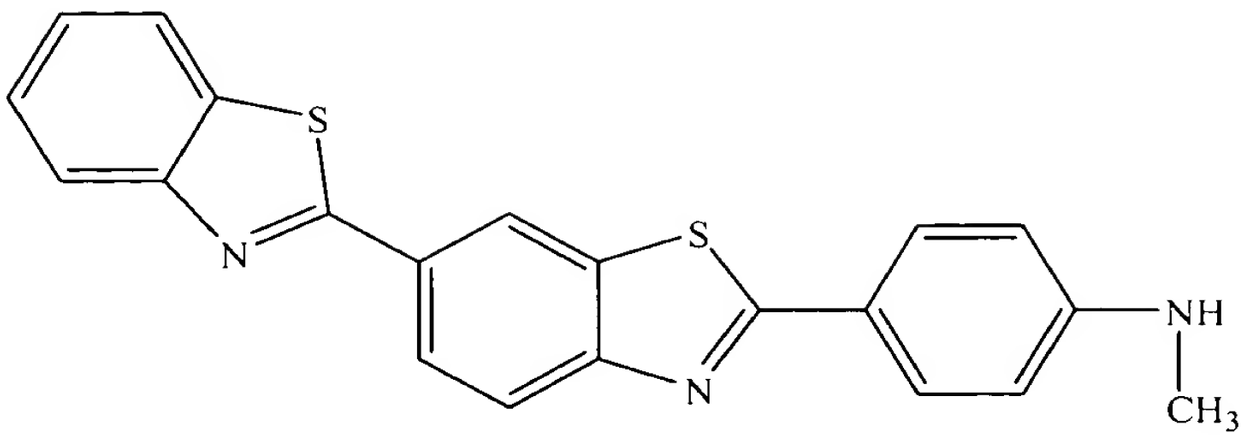


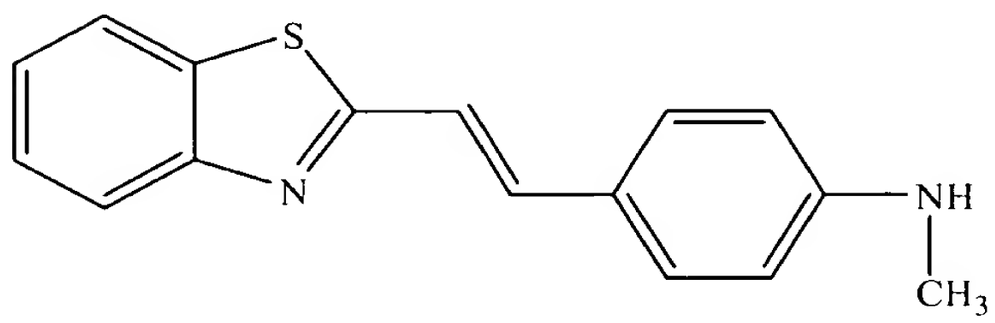
Claim 104:

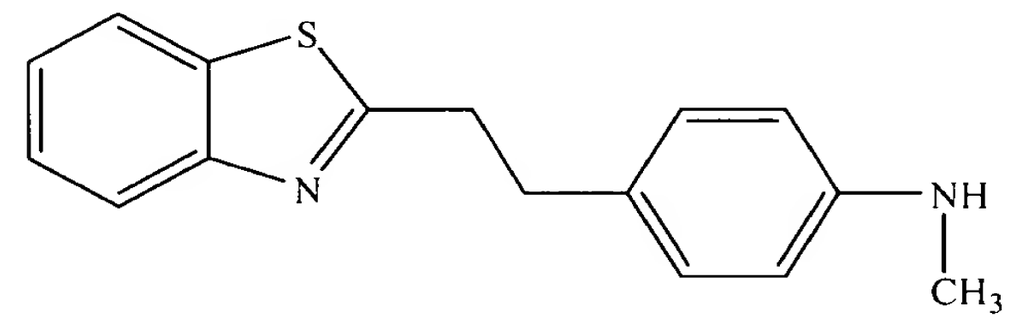


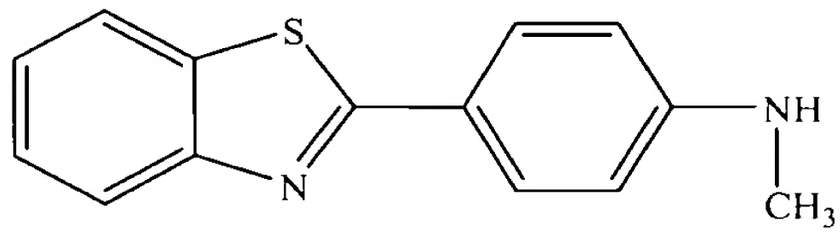
Thus, it is respectfully requested that the Examiner at least search and examine the above two species which are encompassed by the genus of claim 84. Should the Examiner find those species allowable, then it is requested that she extend her search according to MPEP 803.02 which would require a search of the Markush type claim, i.e., claim 84.

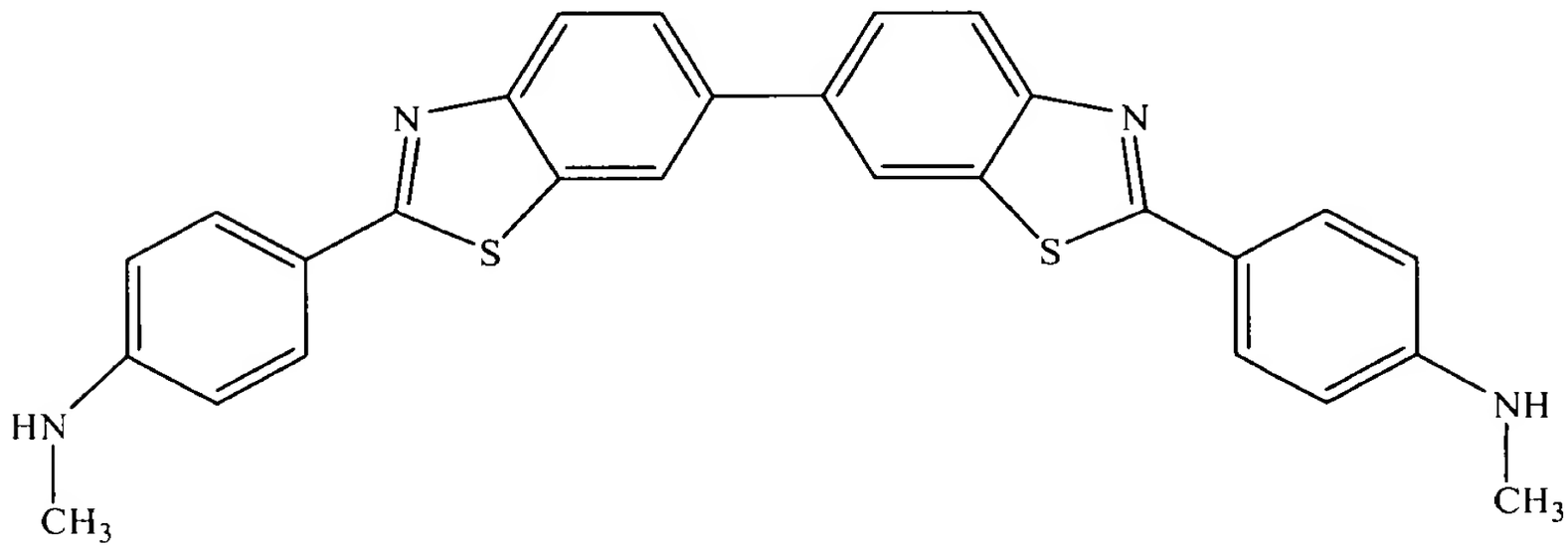
Furthermore, on page 3, the Examiner states "Applicant is reminded that the claims are directed to species which are not enumerated anywhere in the disclosure." Contrary to the Examiner's position, original claims 5-12 are directed to species of the present invention. For example, claim 5 is directed to the following species:











Applicants elected compounds of structure D, where Z is S and have presented new claims directed thereto. The fourth species in original claim 5 corresponds to new claim 91. Therefore, contrary to the Examiner's position, as stated on page 3 of the Office Action "in expanding the search from the elected species to another species, the Examiner may expand the search to any species encompassed by the claims," the species set forth in claims 91-110

are enumerated in the disclosure, as seen in original claims 5-12 and in paragraph 30. Accordingly, it is requested that the Examiner expand the search to include at least the species of claims 91 and 104 and then follow the procedure of MPEP 803.02 to expand the search. In order to assist the Examiner in searching the species claims, attached hereto are chemical structural representations of claims 91-110.

B. Withdrawn Claims

The Examiner has withdrawn claims 78-80, 82, 83, 85-105, 107-110, 11, 115, 116 and 125-130 as directed to a non-elected species/invention. In view of the above arguments, it is respectfully requested that the withdrawn claims be included in the claims presently under examination. At a minimum, it is requested that at least the species claims 91-105 and 107-110 be searched and examined.

C. Rejections based on 35 U.S.C. 103

Claims 81 and 117-123 have been rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over VITEK (U.S. Patent No. 5,935,927). Applicants respectfully traverse.

The Examiner states that Vitek discloses the use of 2-(4-aminophenyl)6-methylbenzothiazole in combination with bis(trichloromethyl)carbonate and xylene in generating an advanced glycosylation end product modified thioflavin. The Examiner states that the structure of 2-(4-aminophenyl)-6-methylbenzothiazole is encompassed in the instant invention when Z is S, Y is NR^1R^2, R^1-R^7 and R^9-R^{10} are H, and R^8 is methyl. The Examiner acknowledges that Vitek does not teach compounds where R^8 is H, ethyl, propyl or butyl. The Examiner concludes that the disclosure of 2-(4-aminophenyl)-6-methylbenzothiazole renders obvious compounds of claim 81, where R^8 is hydrogen based on In re Wood, 199 USPQ 137 (CCPA 1978). The Examiner also concludes that the disclosure of 2-(4-aminophenyl)-6-methylbenzothiazole renders obvious compounds of claim 81, where R^8 is ethyl, propyl or butyl based on the fact that ethyl is the next adjacent homolog (which is next adjacent to propyl, which is next adjacent to butyl) and that members of a homologous series would be expected to have similar properties.

Page 6 of the Office Action summarizes the use of the AGE conjugates in binding assays and other diagnostic tests.

At the outset, the Examiner attention is directed to Example 3. Example 3, column 32, line 41-column 33, line 60 of Vitek discloses that 2-(4-aminophenyl)-6-methylbenzothiazole is a starting material used to prepare 2-(4-[([(6-aminohexyl)aminocarbonyl)amino]phenyl)-6-methylbenzothiazole, which is used in the synthesis of (4-[([(6-[(1-deoxy-2,3:4,5-di-O-isopropylidene-β-D-fructopyranose-1-yl)amino]hexyl)amino]carbonyl)amino]phenyl)-6-methylbenzothiazole, which is used to prepare (4-[(6-[6-[(1-deoxy-β-D-fructopyranos-1-yl)amino]hexyl)amino]carbonyl)amino]-phenyl)-6-methylbenzothiazole. It is this compound, ((4-[(6-[6-[(1-deoxy-β-D-fructopyranos-1-yl)amino]hexyl)amino]carbonyl)amino]-phenyl)-6-methylbenzothiazole), to which an AGE can be conjugated and could be used in the methods the Examiner describes on page 6 of the Office Action.

Vitek also discloses column 34, line 10-column 37, line 40 (also Example 3) that 2-(4-aminophenyl)-6-methylbenzothiazole is a starting material used to prepare 2-[4-(4-phthalimidobutyl)aminophenyl]-6-methylbenzothiazole, which is reacted with hydrazime hydrate to yield 2-[4-(4-aminobutyl)aminophenyl]-6-methylbenzothiazole, which is used to prepare (4-[(4-[(1-deoxy-2,3:4,5-di-O-isopropylidene-β-D-fructopyranos-1-yl)amino]butyl)amino]phenyl)-6-methylbenzothiazole, which was used to prepare (4-[N-(4-N-(1-deoxy-2,3:4,5-di-O-isopropylidene-β-D-fructopyranos-1-y l)-N, N-dimethylammonio!butyl)-amino!phenyl)-6-methylbenzothiazole iodide, which was then used to prepare (4-N-(4-N-(1-deoxy-β-D-fructopyranos-1-yl)-N,N-dimethylammonio]butyl)amino]phenyl)-6-methylbenzothiazole chloride. It is this compound, (4-N-(4-N-(1-deoxy-β-D-fructopyranos-1-yl)-N,N-dimethylammonio]butyl)amino]phenyl)-6-methylbenzothiazole chloride, to which Vitek describes conjugating an Amadori product, which is used to co-precipitate β-amyloid *in vitro*.

For a proper *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art references (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the

reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure. See MPEP 2142.

With respect to the first prong, the Examiner relies on the disclosure of 2-(4-amiophenyl)-6-methylbenzothiazole as a starting material in Vitek to teach that an allegedly structurally similar compound, i.e. a compound of claim 81, wherein R^8 is H, is obvious and cites to In re Wood, 199 USPQ 137 (CCPA 1978). The Court of Appeals in Wood affirmed the PTO Board of Patent Appeals and Interferences holding that the claimed compounds of Wood were prima facie obvious over the cited reference because of the close structural similarity **and** because the prior art compound taught the same activity[1]. In the present case, the compound the Examiner cites is a starting material used in a multi-step synthesis to yield a product which is conjugated to an AGE which can then be used for enhancing removal of amyloid from a peripheral tissue. In the present case, Vitek fails to disclose any activity for 2-(4-aminophenyl)-6-methylbenzothiazole. Thus, the holding in Wood is inapplicable here since the Court of Appeals in Wood affirmed the PTO's finding of obviousness based on prior art compounds have structural similarity **and** similar activity. MPEP 2144.08 states that in a proper *prima facie* case of obviousness, the Examiner must consider the teaching of similar properties or uses. MPEP 2144.08 further states, "close structural similarity alone is not sufficient to create a *prima facie* case of obviousness when the reference compounds lack utility, and thus there is no motivation to make related compounds." In re Stemniski, 170 USPQ 343 (CCPA 1971). Based on the fact that Vitek uses 2-(4-aminophenyl)-6-methylbenzothiazole as a starting material and only discloses the end product of the synthesis as being conjugated to an AGE which is useful for enhancing removal of amyloid, motivation to replace the methyl of Vitek with a hydrogen for the R^8 position is lacking. Since, motivation to modify the Vitek compound is lacking, a proper case of *prima facie* obviousness has not been set forth.

Assuming that sufficient motivation was present, the case of *prima facie* obviousness falls on the remaining two parts of the test, reasonable expectation of success and the prior art reference teaching or suggesting all the claim limitations. Since the material of Vitek is a

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[1] Wood claimed 7,7-di-alkyl derivatives of pteridine which were active as antimicrobial agents and the cited prior art to Mitsuda disclosed the unsubstituted analogs having antimicrobial properties.

starting material, there is no reasonable expectation of success to modify the Vitek compound since no biological properties shown or described. With respect to the prior art reference teaching all the claim limitations, the prior art fails to teach or suggest compounds where R^8 is hydrogen. Therefore, based on the holding in Wood and the lack of teaching of Vitek, a proper *prima facie* case of obviousness has not been established.

The Examiner has also held that compounds of claim 81, wherein R^8 is ethyl, propyl or butyl are obvious over the disclosure of 2-(4-aminophenyl)-6-methylbenzothiazole as a starting material in Vitek. In sum, the Office Action states that one skilled in the art would recognize that characteristics of a homologous series of compounds would be similar and as such, one member of that series renders other members obvious. The basis for the Examiner's position appears to come from In re Payne, 203 USPQ 245 (CCPA 1979). Payne holds that members of a homologous series are expected to have similar properties and without further secondary considerations of unexpected results are obvious over each other. In the present application, Applicants claim compounds where R^8 can be ethyl, propyl or butyl. The Examiner has rejected claim 81 based on this definition of R^8 over Vitek's disclosure of 2-(4-aminophenyl)-6-methylbenzothiazole, i.e., R^8 is methyl. However, as noted above, Vitek uses 2-(4-aminophenyl)-6-methylbenzothiazole as a starting material and does not disclose any property of 2-(4-aminophenyl)-6-methylbenzothiazole. The court in Payne points out, "[a]n obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a claimed compound, **in the expectation that compounds similar in structure will have similar properties**." Payne at 254 (Emphasis added). Vitek does not disclose any properties of 2-(4-aminophenyl)-6-methylbenzothiazole, therefore, one skilled in the art would have no expectations with respect to the claimed invention in claim 81 where R^8 is ethyl, propyl or butyl. There is no motivation to modify 2-(4-aminophenyl)-6-methylbenzothiazole to arrive at the claimed invention where R^8 is ethyl, propyl or butyl. Based on Payne and the lack of teaching of Vitek, a proper *prima facie* case of obviousness has not been established.

Accordingly, based on the above arguments, reconsideration and withdrawal of the rejection are respectfully requested.

III. CONCLUSION

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date Oct. 28, 2003

By _____

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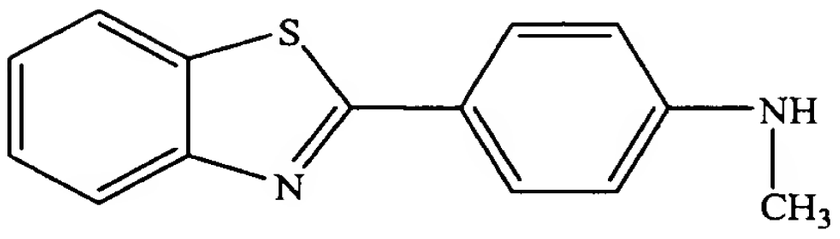
Mary C. Till
Attorney for Applicant
Registration No. 41,545

Structural Representations of Claims 91-110

91.



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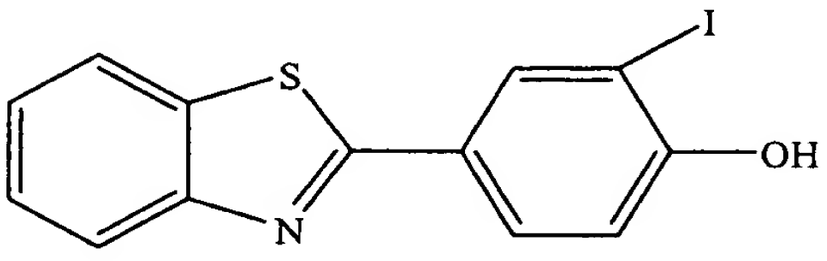

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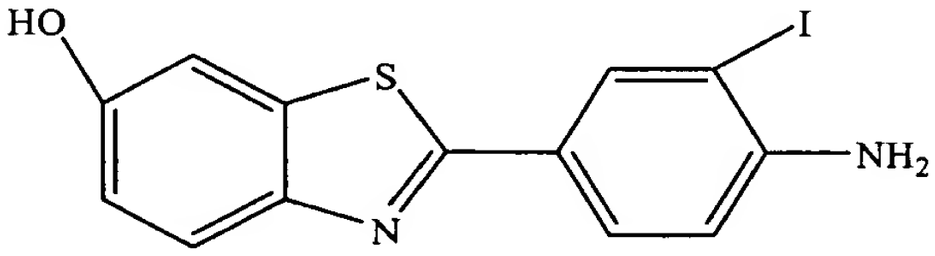

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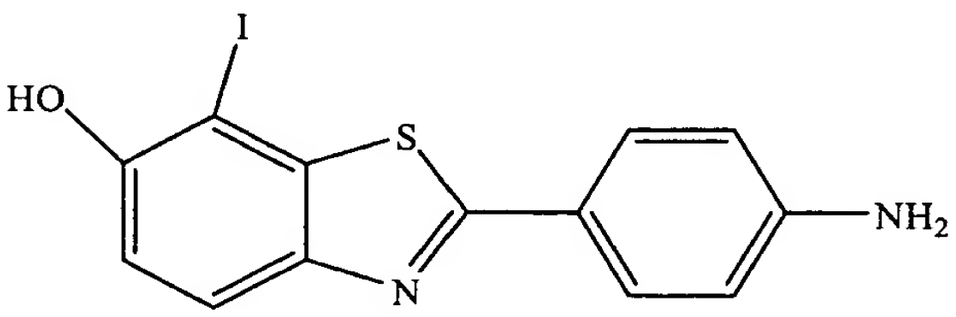

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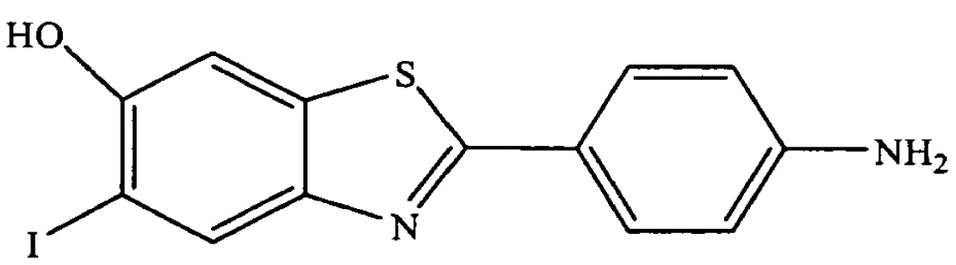

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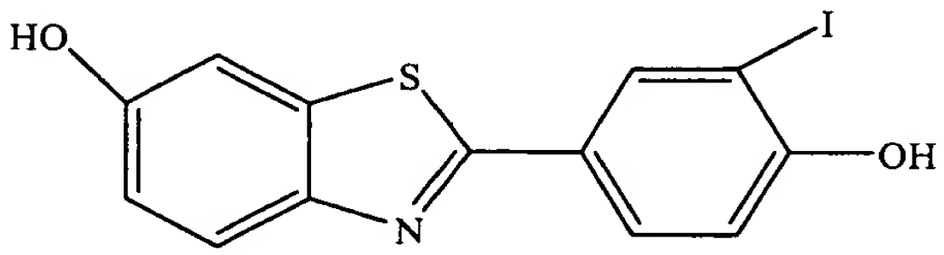

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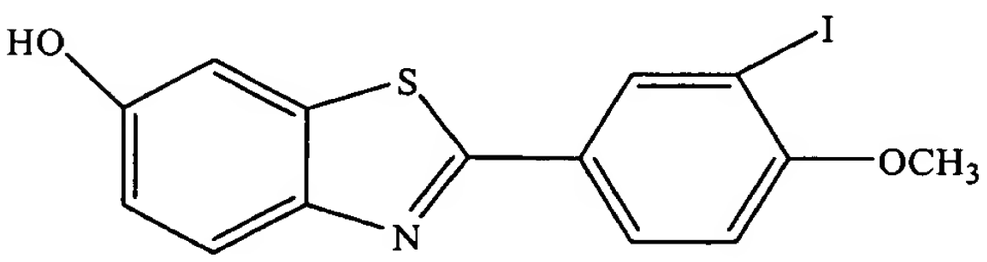

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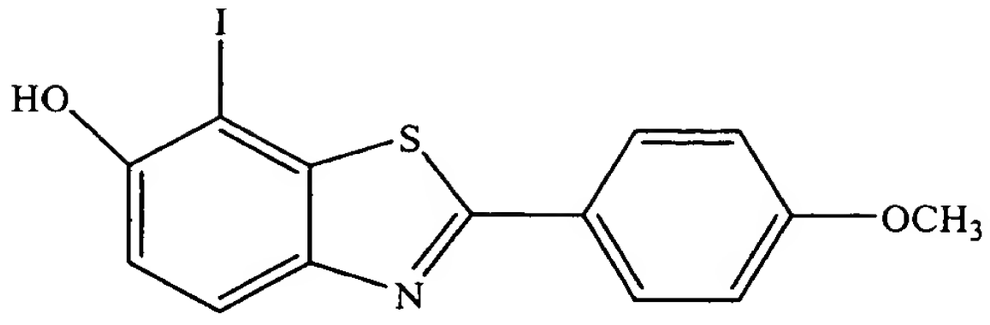

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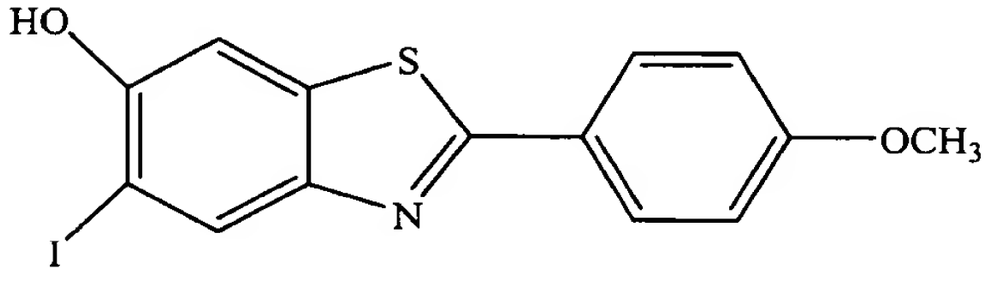

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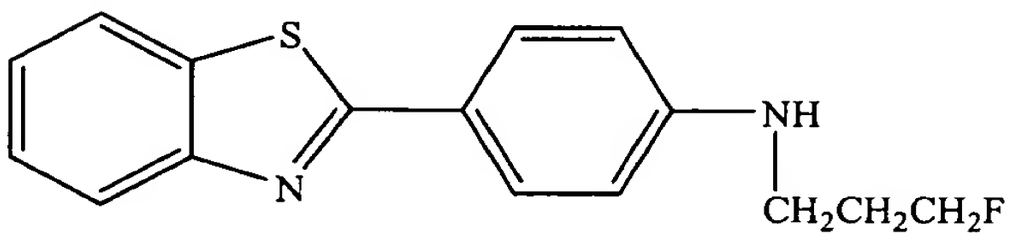

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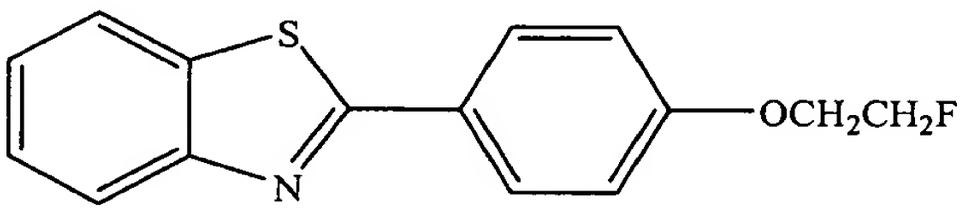

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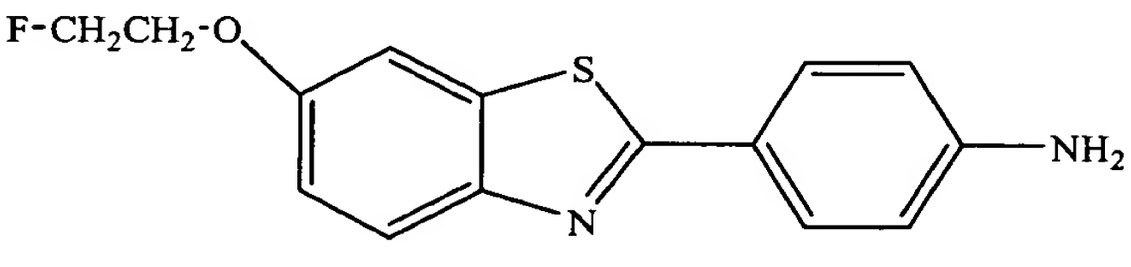

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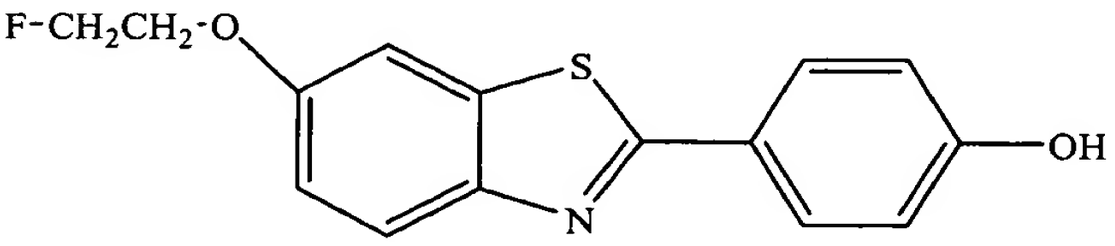
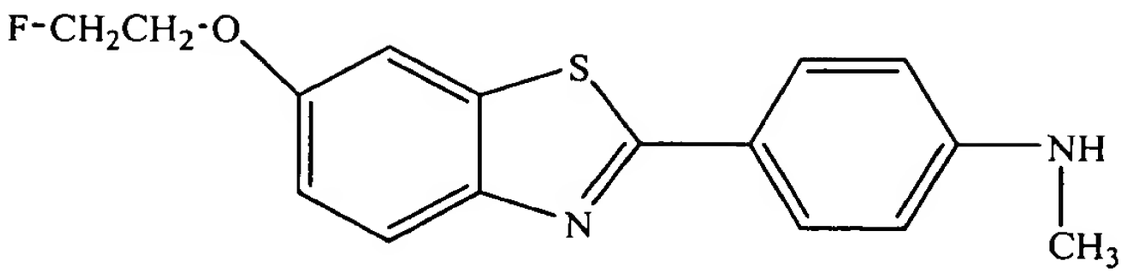
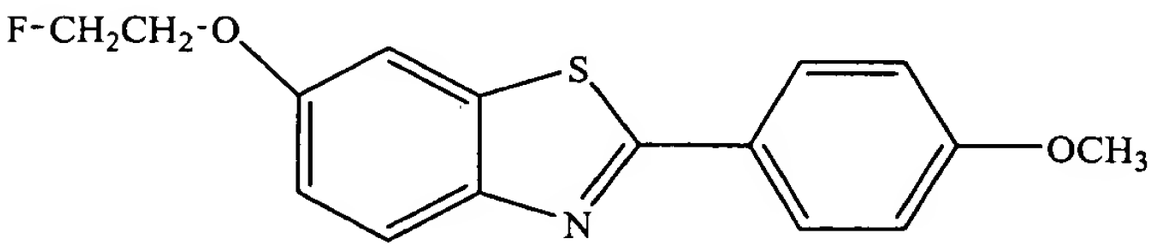
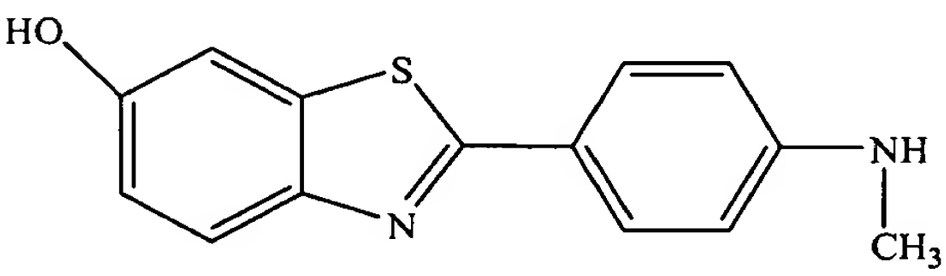
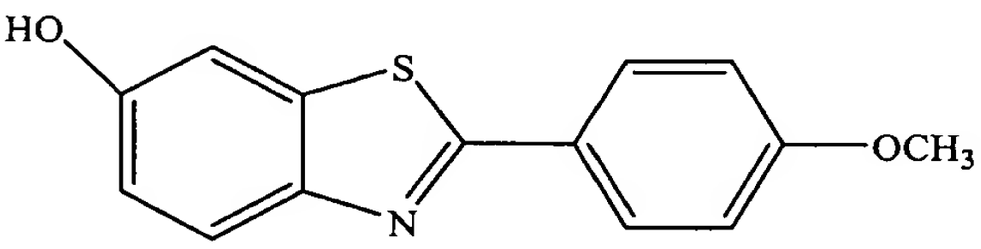
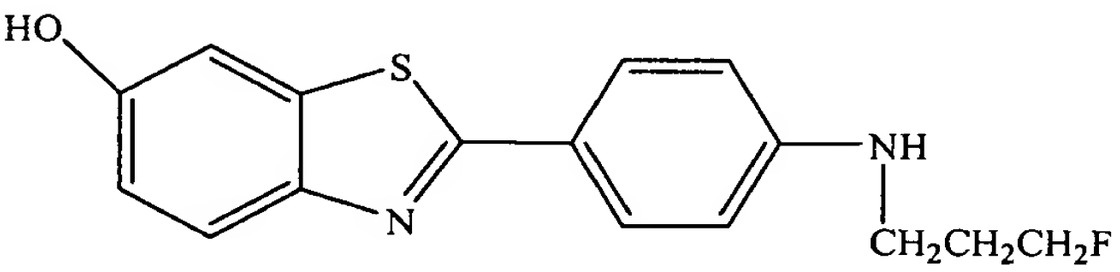


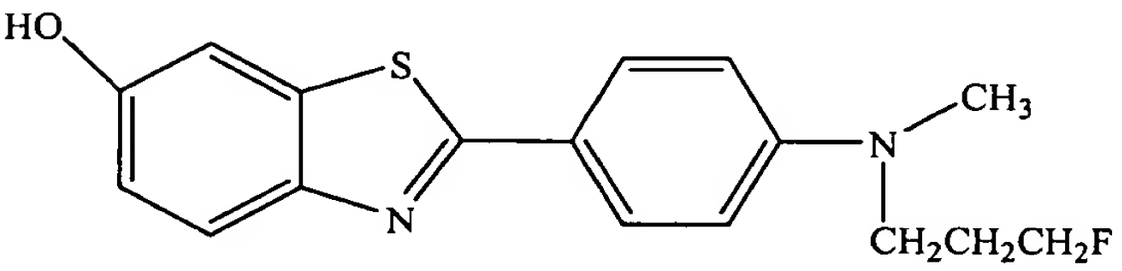
104. 

105. 

106. 

107. 

108. 

109. 

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